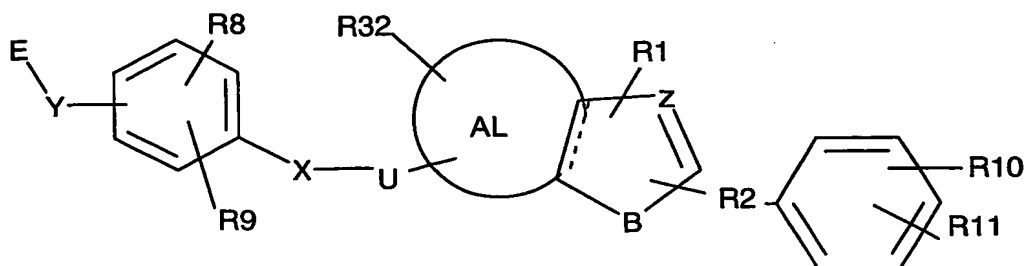


CLAIMS

What is claimed is:

1. A compound of the structural Formula I':



5

and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- 10 (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- 15 (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and
- 20
- 25

S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

- 5 (c) R2 is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;
- (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;
- 10 (e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is optionally substituted with from one to four substituents each independently selected from R30;
- 15 (f) Y is selected from the group consisting of C, NH, and a single bond;
- (g) E is C(R3)(R4)A or A and wherein
- (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and
- 20 tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;
- (ii) each R⁷ is independently selected from the
- 25 group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;
- (iii) R3 is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and
- (iv) R4 is selected from the group consisting of
- 30 H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4

are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R₂₆;

(h) B is selected from the group consisting of S, O, C, and N;

(i) Z is selected from the group consisting of N and C, with the proviso that when B is C then Z is N;

(j) R₈ is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;

(k) R₉ is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR₂₉, and OR₂₉, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R₂₇; R₂₉ is selected from the group consisting of hydrogen, C₁-C₄ alkylenyl, and C₁-C₄ alkyl; R₈ and R₉ optionally combine to form a five membered fused bicyclic with the phenyl to which R₈ and R₉ attach, provided that when R₈ and R₉ form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R₈ and R₉ fused bicyclic;

(l) R₁₀, R₁₁ are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-₄-alkyl, aryl-C₁-₄-heteroalkyl, heteroaryl-C₀-₄-alkyl, C₃-C₆ cycloalkylaryl-C₀-₂-alkyl, aryloxy, C(O)R₁₃' ,

COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂,
NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23',
S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀-
4-alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀-4-
5 alkyl, and C3-C6 cycloalkylaryl-C₀-2-alkyl are

each optionally substituted with from one to three
substituents independently selected from R28;

(m) R12', R12'', R13', R14', R15', R16', R17', R18',
R19', R20', R21', R22', R23', R24', and R25' are

10 each independently selected from the group
consisting of hydrogen, C₁-C₆ alkyl and aryl;

(n) R30 is selected from the group consisting of C₁-C₆
alkyl, aryl-C₀-4-alkyl, aryl- C₁₋₄-heteroalkyl,
heteroaryl-C₀-4-alkyl, and C3-C6 cycloalkylaryl-
15 C₀-2-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀-4-
alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀-4-
alkyl, and C3-C6 cycloalkylaryl-C₀-2-alkyl are

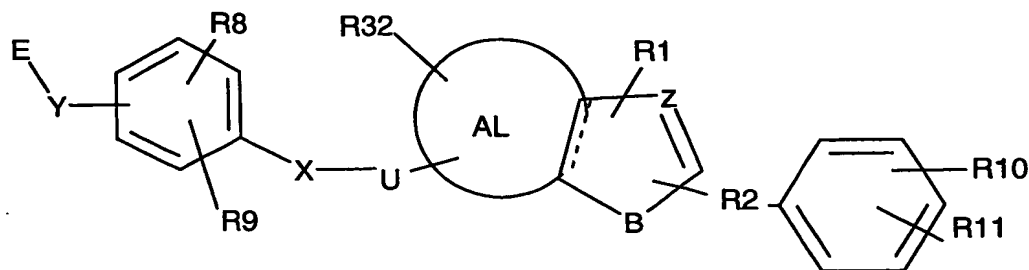
each optionally substituted with from one to three
substituents each independently selected from R31;

20 (o) R32 is selected from the group consisting of a
bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl,
and C₁-C₆ alkyloxo;

(p) AL is selected from the group consisting of a
fused C₃-C₈ carbocyclic, a fused pyridinyl, a
25 fused pyrimidinyl, and a fused phenyl; and

(q) ---- is optionally a bond to form a double bond at
the indicated position.

2. A compound of the structural Formula I'':



and stereoisomers, pharmaceutically acceptable salts,
5 solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉, NR₂₀SO₂R₂₁, SR₂₂, S(O)R₂₃, S(O)₂R₂₄, and S(O)₂N(R₂₅)₂; R₁₂, R₁₃, R₁₄, R₁₅, R₁₆, R₁₇, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₃, R₂₄ and R₂₅ are each

independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

(c) R₂ is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;

5 (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;

(b) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker is substituted with from one to four substituents each independently selected from R₃₀;

10 (e) Y is selected from the group consisting of C, O, S, NH and a single bond;

(f) E is C(R₃)(R₄)A or A and wherein

15 (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with from one to two groups independently selected from R⁷;

20 (ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

25 (iii) R₃ is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and

(iv) R₄ is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R₃ and R₄ are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy,

30

cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

- (g) B is selected from the group consisting of S, O, C, and N;
- (h) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;
- (i) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;
- (j) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR29, and OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R27; R29 is selected from the group consisting of hydrogen, C₁-C₄ alkylenyl, and C₁-C₄ alkyl; R8 and R9 optionally combine to form a five membered fused bicyclic with the phenyl to which R8 and R9 attach, provided that when R8 and R9 form a fused ring, the group E-Y- is bonded at any available position on the five membered ring of such R8 and R9 fused bicyclic;
- (k) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23',

S(O)₂R₂₄' , and S(O)₂N(R₂₅')₂; and wherein aryl-C₀-
4-alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-
alkyl, and C₃₋₆ cycloalkylaryl-C₀₋₂-alkyl are
each optionally substituted with from one to three
substituents independently selected from R₂₈;

(l) R₁₂' , R₁₂'', R₁₃' , R₁₄' , R₁₅' , R₁₆' , R₁₇' , R₁₈' ,
R₁₉' , R₂₀' , R₂₁' , R₂₂' , R₂₃' , R₂₄' , and R₂₅' are
each independently selected from the group
consisting of hydrogen, C₁₋₆ alkyl and aryl;

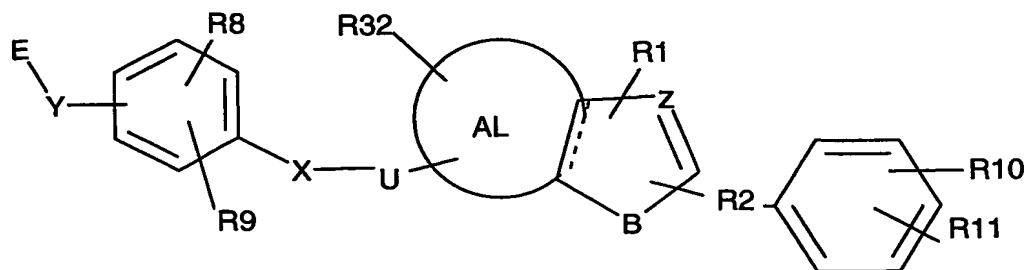
(m) R₃₀ is selected from the group consisting of C₁₋₆
alkyl, aryl-C₀₋₄-alkyl, aryl- C₁₋₄-heteroalkyl,
heteroaryl-C₀₋₄-alkyl, and C₃₋₆ cycloalkylaryl-
C₀₋₂-alkyl, and wherein C₁₋₆ alkyl, aryl-C₀₋₄-
alkyl, aryl- C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-
alkyl, and C₃₋₆ cycloalkylaryl-C₀₋₂-alkyl are
each optionally substituted with from one to three
substituents each independently selected from R₃₁;

(n) R₃₂ is selected from the group consisting of a
bond, hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl,
and C₁₋₆ alkyloxo;

(o) AL is selected from the group consisting of a
fused C₃₋₈ carbocyclic, a fused pyridinyl, a
fused pyrimidinyl, and a fused phenyl; and

(p) ---- is optionally a bond to form a double bond at
the indicated position.

3. A compound of the structural Formula I''':



and stereoisomers, pharmaceutically acceptable salts,
 5 solvates and hydrates thereof, wherein:

- (a) R1 is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R1';
- (b) R1', R26, R27, R28 and R31 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R13, COOR14, OC(O)R15, OS(O)₂R16, N(R17)₂, NR18C(O)R19, NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18, R19, R20, R21, R22, R23, R24 and R25 are each

independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;

(c) R₂ is selected from the group consisting of C₀-C₈ alkyl and C₁₋₄-heteroalkyl;

5 (d) X is selected from the group consisting of a single bond, O, S, S(O)₂ and N;

(e) U is an aliphatic linker wherein one carbon atom of the aliphatic linker is optionally replaced with O, NH or S, and wherein such aliphatic linker
10 is optionally substituted with from one to four substituents each independently selected from R₃₀;

(f) Y is selected from the group consisting of C, O, S, NH and a single bond;

(g) E is C(R₃)(R₄)A or A and wherein

15 (i) A is selected from the group consisting of carboxyl, tetrazole, C₁-C₆ alkyl nitrile, carboxamide, sulfonamide and acylsulfonamide; wherein sulfonamide, acylsulfonamide and tetrazole are each optionally substituted with
20 from one to two groups independently selected from R⁷;

(ii) each R⁷ is independently selected from the group consisting of hydrogen, C₁-C₆ haloalkyl, aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

25 (iii) R₃ is selected from the group consisting of hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and

(iv) R₄ is selected from the group consisting of H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl, and aryl C₀-C₄ alkyl, and R₃ and R₄
30 are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy,

cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R26;

with the proviso that when Y is O then R4 is

5 selected from the group consisting of C₁-C₅

alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆ cycloalkyl,

and aryl C₀-C₄ alkyl, and R3 and R4 are

optionally combined to form a C₃-C₄ cycloalkyl,

and wherein alkyl, alkoxy, cycloalkyl and aryl-

10 alkyl are each optionally substituted with one

to three each independently selected from R26;

(h) B is selected from the group consisting of S, O, C, and N;

(i) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;

(j) R8 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;

(k) R9 is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-

20 C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, SR29, and

OR29, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three

independently selected from R27; R29 is selected

from the group consisting of hydrogen, C₁-C₄

25 alkylenyl, and C₁-C₄ alkyl; R8 and R9 optionally

combine to form a five membered fused bicyclic

with the phenyl to which R8 and R9 attach,

provided that when R8 and R9 form a fused ring,

the group E-Y- is bonded at any available position

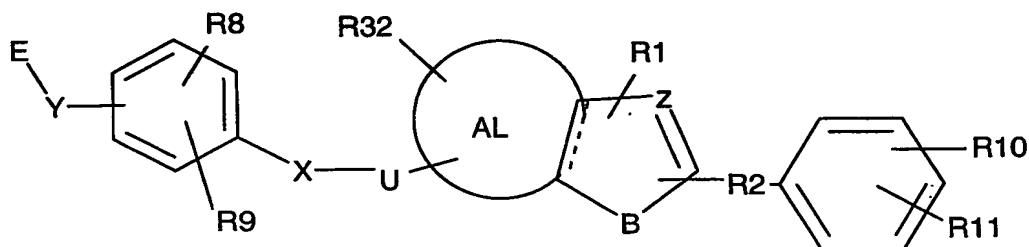
30 on the five membered ring of such R8 and R9 fused

bicyclic;

- (1) R10, R11 are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, aryloxy, C(O)R13', COOR14', OC(O)R15', OS(O)₂R16', N(R17')₂, NR18'C(O)R19', NR20'SO₂R21', SR22', S(O)R23', S(O)₂R24', and S(O)₂N(R25')₂; and wherein aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R28;
- (m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁-C₆ alkyl and aryl;
- (n) R30 is selected from the group consisting of C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and wherein C₁-C₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;
- (o) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, and C₁-C₆ alkyloxo;

- (p) AL is selected from the group consisting of a fused C₃-C₈ carbocyclic, a fused pyridinyl, a fused pyrimidinyl, and a fused phenyl; and
- (q) ---- is optionally a bond to form a double bond at the indicated position.

4. A compound of the Formula I:



and stereoisomers, pharmaceutically acceptable salts, solvates and hydrates thereof, wherein:

- (a) R₁ is selected from the group consisting of hydrogen, C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl, and, wherein C₁-C₈ alkyl, C₁-C₈ alkenyl, aryl-C₀-4-alkyl, aryl-C₁-4-heteroalkyl, heteroaryl-C₀-4-alkyl, C₃-C₆ cycloalkylaryl-C₀-2-alkyl are each optionally substituted with from one to three substituents independently selected from R₁';
- (b) R₁', R₂₆, R₂₇, R₂₈ and R₃₁ are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂, C₁-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryloxy, aryl-C₀-4-alkyl, heteroaryl, heterocycloalkyl, C(O)R₁₃, COOR₁₄, OC(O)R₁₅, OS(O)₂R₁₆, N(R₁₇)₂, NR₁₈C(O)R₁₉,

NR20SO₂R21, SR22, S(O)R23, S(O)₂R24, and
S(O)₂N(R25)₂; R12, R13, R14, R15, R16, R17, R18,
R19, R20, R21, R22, R23, R24 and R25 are each
independently selected from the group consisting
of hydrogen, C₁-C₆ alkyl and aryl;

(c) R2 is selected from the group consisting of C₀-C₈
alkyl and C₁₋₄-heteroalkyl;

(d) X is selected from the group consisting of a
single bond, O, S, S(O)₂ and N;

(e) U is an aliphatic linker wherein one carbon atom
of the aliphatic linker may be replaced with O, NH
or S, and wherein such aliphatic linker is
optionally substituted with R30;

(f) Y is selected from the group consisting of C, O,
S, NH and a single bond;

(g) E is C(R3)(R4)A or A and wherein

(i) A is selected from the group consisting of
carboxyl, tetrazole, C₁-C₆ alkyl nitrile,
carboxamide, sulfonamide and acylsulfonamide;
wherein sulfonamide, acylsulfonamide and
tetrazole are each optionally substituted with
from one to two groups independently selected
from R⁷;

(ii) each R⁷ is independently selected from the
group consisting of hydrogen, C₁-C₆ haloalkyl,
aryl C₀-C₄ alkyl and C₁-C₆ alkyl;

(iii) R3 is selected from the group consisting of
hydrogen, C₁-C₅ alkyl, and C₁-C₅ alkoxy; and

(iv) R4 is selected from the group consisting of
H, C₁-C₅ alkyl, C₁-C₅ alkoxy, aryloxy, C₃-C₆
cycloalkyl, and aryl C₀-C₄ alkyl, and R3 and R4

are optionally combined to form a C₃-C₄ cycloalkyl, and wherein alkyl, alkoxy, aryloxy, cycloalkyl and aryl-alkyl are each optionally substituted with one to three substituents each independently selected from R₂₆;

- (h) B is selected from the group consisting of S, O, C, and N, with the proviso that when B is N then Z is C;
- (i) Z is selected from the group consisting of N and C; with the proviso that when B is C then Z is N;
- (j) R₈ is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, and halo;
- (k) R₉ is selected from the group consisting of hydrogen, C₁-C₄ alkyl, C₁-C₄ alkylenyl, halo, aryl-C₀-C₄ alkyl, heteroaryl, C₁-C₆ allyl, and OR₂₉, and wherein aryl-C₀-C₄ alkyl, heteroaryl are each optionally substituted with from one to three independently selected from R₂₇; R₂₉ is selected from the group consisting of hydrogen and C₁-C₄ alkyl;
- (l) R₁₀, R₁₁ are each independently selected from the group consisting of hydrogen, hydroxy, cyano, nitro, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR₁₂'', C₀-C₆ alkoxy, C₁-C₆ haloalkyl, C₁-C₆ haloalkyloxy, C₃-C₇ cycloalkyl, aryl-C₀-₄-alkyl, aryl-C₁-₄-heteroalkyl, heteroaryl-C₀-₄-alkyl, C₃-C₆ cycloalkylaryl-C₀-₂-alkyl, aryloxy, C(O)R₁₃', COOR₁₄', OC(O)R₁₅', OS(O)₂R₁₆', N(R₁₇')₂, NR₁₈'C(O)R₁₉', NR₂₀'SO₂R₂₁', SR₂₂', S(O)R₂₃', S(O)₂R₂₄', and S(O)₂N(R₂₅')₂; and wherein aryl-C₀-₄-alkyl, aryl-C₁-₄-heteroalkyl, heteroaryl-C₀-₄-

alkyl, and C3-C6 cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents independently selected from R28;

(m) R12', R12'', R13', R14', R15', R16', R17', R18', R19', R20', R21', R22', R23', R24', and R25' are each independently selected from the group consisting of hydrogen, C₁₋₆ alkyl and aryl;

(n) R30 is selected from the group consisting of C₁₋₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C3-C6 cycloalkylaryl-C₀₋₂-alkyl, and wherein C₁₋₆ alkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, and C3-C6 cycloalkylaryl-C₀₋₂-alkyl are each optionally substituted with from one to three substituents each independently selected from R31;

(o) R32 is selected from the group consisting of a bond, hydrogen, halo, C₁₋₆ alkyl, C₁₋₆ haloalkyl, and C₁₋₆ alkyloxy;

(p) AL is selected from the group consisting of a fused C₃₋₈ carbocyclic and a fused phenyl; and

(q) ---- is optionally a bond to form a double bond at the indicated position.

5. A compound as claimed by Claim 1 wherein X is -O-.

6. A compound as claimed by Claims 1 wherein X is -S.

7. A compound as claimed by any one of Claims 1 through 6 wherein Y is O.

8. A compound as claimed by any one of Claims 1 through 6 wherein Y is C.

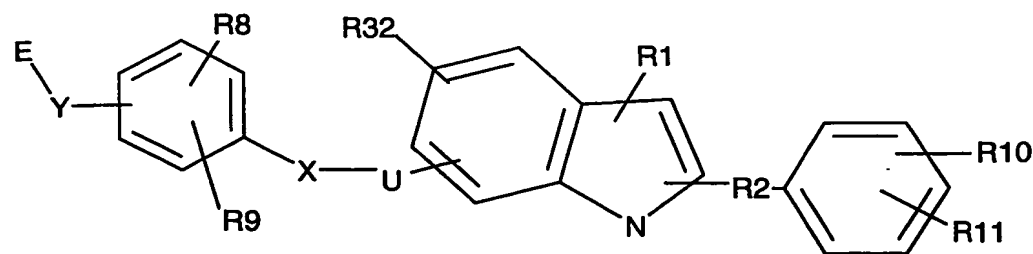
9. A compound as claimed by any one of Claims 1 through 6 wherein Y is S.

10. A compound as claimed by any one of Claims 1 through 9 wherein Z is N.
11. A compound as claimed by any one of Claims 1 through 9 wherein B is S or O.
- 5 12. A compound as claimed by any one of Claims 1 through 9, wherein B is N.
13. A compound as claimed by any one of Claims 1 through 9 wherein Z is N.
- 10 14. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused phenyl.
- 15 15. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused cycloalkyl.
16. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused pyrimidinyl.
- 15 17. A compound as claimed by any one of Claims 1 through 13 wherein AL is a fused pyridinyl.
18. A compound as claimed by any one of Claims 1 through 13 or Claim 15 wherein ---- is a bond to form a double bond at the designated location on Formula I.
- 20 19. A compound as claimed by any one of Claims 1 through 18 wherein E is C(R3)(R4)A.
20. A compound as claimed by any one of Claims 1 through 18 wherein E is A.
- 25 21. A compound as claimed by any one of Claims 1 through 19 wherein A is COOH.
22. A compound as claimed by any one of Claims 1 through 21 wherein R10 is haloalkyl.
23. A compound as claimed by any one of Claims 1 through 22 wherein R10 is CF₃.
- 30 24. A compound as claimed by any one of Claims 1 through 21 wherein R10 is haloalkyloxy.

25. A compound as claimed by any one of Claims 1 through 21 wherein R10 and R11 are each independently selected from the group consisting of hydrogen, halo, oxo, C₁-C₆ alkyl, C₁-C₆ alkyl-COOR12'', C₁-C₆ alkoxy, C₁-C₆ haloalkyl, and C₁-C₆ haloalkyloxy.
26. A compound as claimed by any one of Claims 1 through 21 wherein R10 is selected from the group consisting of C₃-C₇ cycloalkyl, aryl-C₀₋₄-alkyl, aryl-C₁₋₄-heteroalkyl, heteroaryl-C₀₋₄-alkyl, C₃-C₆ cycloalkylaryl-C₀₋₂-alkyl, and aryloxy.
27. A compound as claimed by any one of Claims 1 through 26 wherein R8 is selected from the group consisting of C₁-C₃ alkyl and C₁-C₄ alkylenyl.
28. A compound as claimed by any one of Claims 1 through 26, wherein R8 and R9 are each independently selected from the group consisting of hydrogen and C₁-C₃ alkyl.
29. A compound as claimed by any one of Claims 1 through 27 wherein R29 is C₁-C₄ alkylenyl.
30. A compound as claimed by any one of Claims 1 through 27 and 29 wherein R8 is C₁-C₄ alkylenyl.
31. A compound as claimed by any one of Claims 1 through 27, 29, and 30 wherein R9 is OR29.
32. A compound as claimed by any one of Claims 1 through 27, 29, and 30 wherein R9 is SR29.
33. A compound as claimed by any one of Claims 1 through 27, 29 through 32 wherein R8 and R9 combine to form a fused bicyclic.
34. A compound as claimed by any one of Claims 1 through 33 wherein R1, R2, R3, and R4 are each

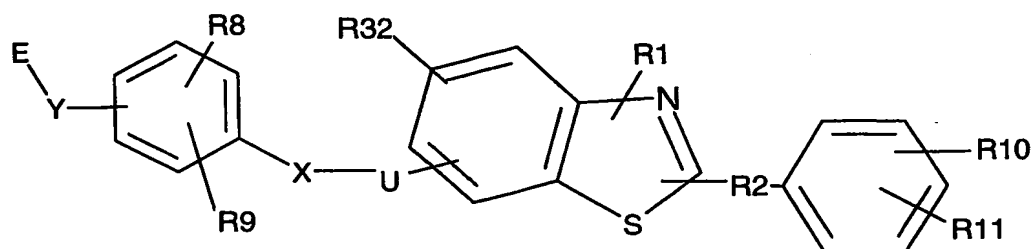
independently selected from the group consisting of C₁-C₂ alkyl.

35. A compound as claimed by any one of Claims 1 through 33 wherein R₁, R₃, and R₄ are each independently selected from the group consisting of hydrogen and C₁-C₂ alkyl.
36. A compound as claimed by any one of Claims 1 through 33 and 35 wherein R₂ is a bond.
37. A compound as claimed by any one of Claims 1 through 36 wherein U is C₁-C₃ alkyl.
38. A compound as claimed by Claim 37 wherein U is saturated.
39. A compound as claimed by any one of Claims 37 or 38 wherein U is substituted with C₁-C₃ alkyl.
40. A compound as claimed by any one of Claims 1 through 39 wherein aliphatic linker is substituted with from one to four substituents each independently selected from the group consisting of R₃₀.
41. A compound as claimed by any one of Claims 1 through 38, 39, and 40 wherein one carbon of the aliphatic linker is replaced with an -O-.
42. A compound as claimed by any one of Claims 1 through 9, 12, 13, 14, Claims 18 through 32, Claims 34 through 41 of the Structural Formula



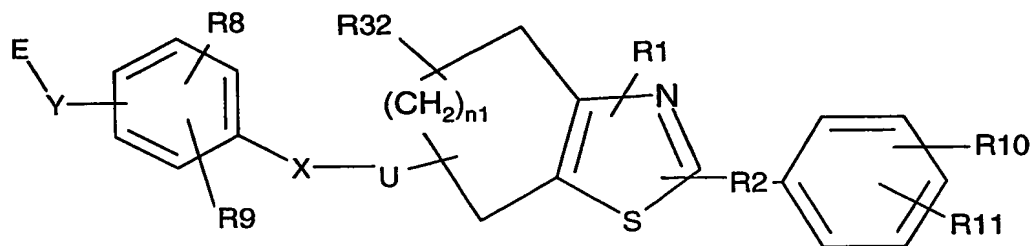
43. A compound as claimed by any one of Claims 1 through 11, 13, 14, Claims 17 through 32, Claims 34 through 41 of the Structural Formula

III:



44. A compound as claimed by any one of Claims 1 through 11, 15, Claims 18 through 32, Claims 34 through 41 of the Structural Formula

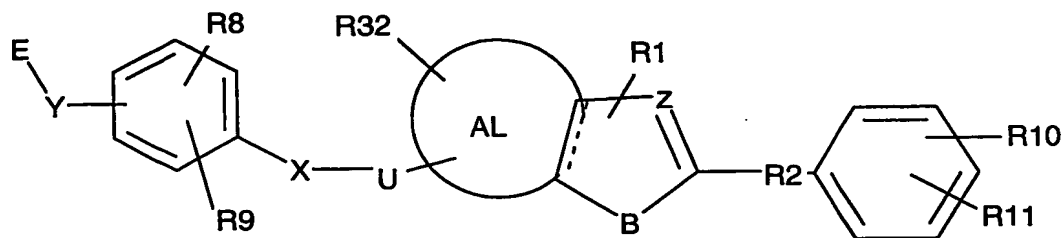
IV:



wherein n1 is 1 to 5.

45. A compound as claimed by any one of Claims 1 through 14, 18 through 32, Claims 34 through 41 of the Structural Formula

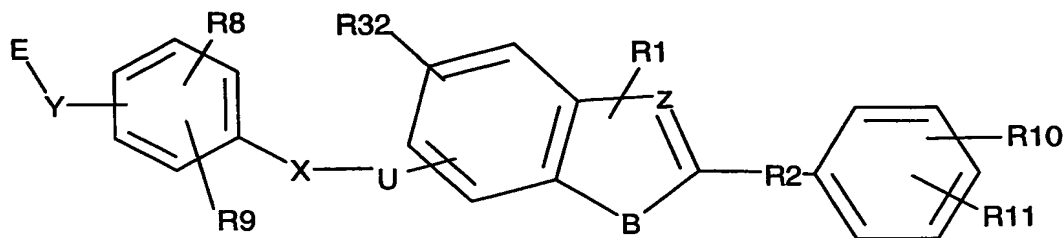
V:



46. A compound as claimed by any one of Claims 1 through 14, Claims 18 through 32 Claims 34 through 41

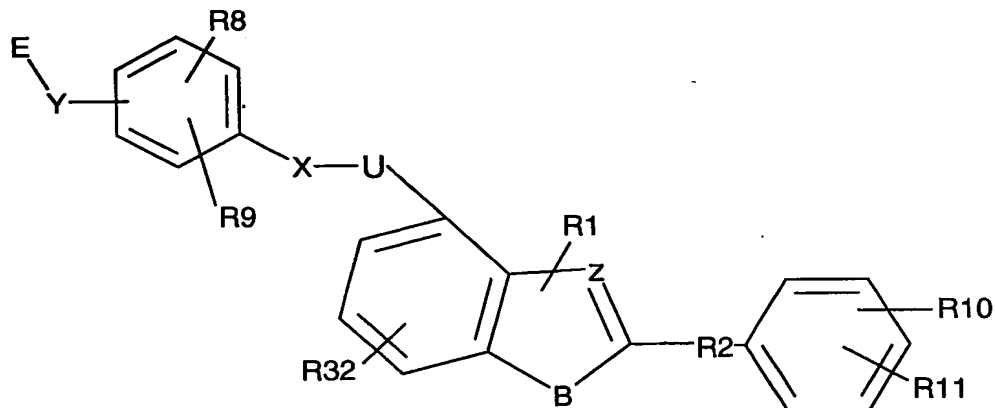
of the Structural Formula

VI:



47. A compound as claimed by any one of Claims 1
5 through 14, Claims 18 through 32, Claims 34 through
41 of the Structural Formula

VII:

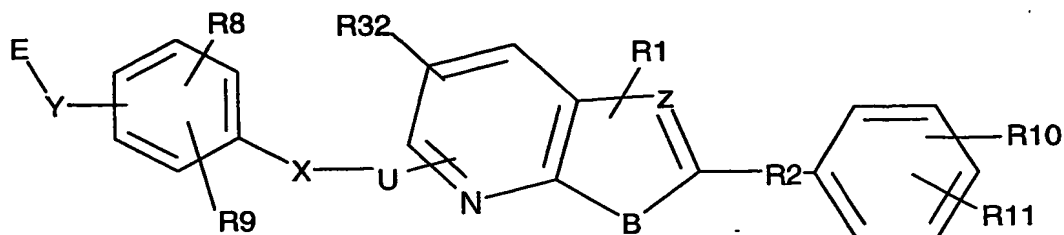


48. A compound as claimed by any one of Claims 1
10 through 14, Claims 18 through 32, Claims 34 through
47 wherein X is S, Y is selected from the group
consisting of C and O, E is CH₂COOH, and R2 is a
bond.

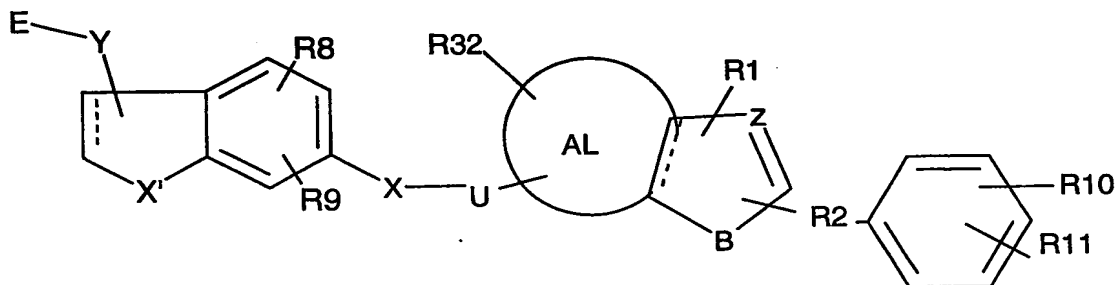
49. A compound as claimed by any one of Claims 1
15 through 11, and Claims 13 through 48, wherein Z is N
and B is S.

50. A compound as claimed by any one of Claims 1
through 49 wherein R32 is hydrogen, R8 is hydrogen
and R9 is C₁-C₄ alkyl.

51. A compound as claimed by any one of Claims 1 through 13, 17, Claims 18 through 32, Claims 34 through 41 of the Structural Formula VIII:

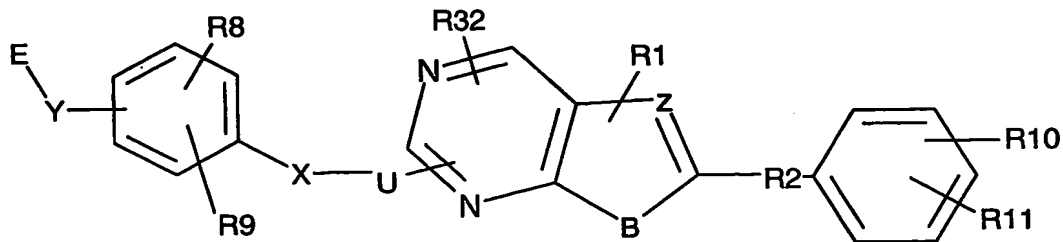


52. A compound as claimed by any one of Claims 1 through 32 Claims 34 through 41 of the Structural Formula IX:



wherein X' is selected from the group consisting of O and S.

53. A compound as claimed by any one of Claims 1 through 13, 16, Claims 18 through 32 Claims 34 through 41 of the Structural Formula X:



54. A compound as claimed by any one of Claims 1 through 4 wherein the compound is selected from the group consisting of

Racemic-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-propionic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

Racemic-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenoxy}-acetic acid;

Racemic-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(S)-{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(R)-{3-[2-(4-Trifluoromethyl-phenyl)-5,6-dihydro-4H-cyclopentathiazol-4-ylmethoxy]-phenyl}-acetic acid;

{2-Methyl-4-[7-methyl-2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;

(R)-{3-[2-(4-Trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-acetic acid;

(S)-{3-[2-(4-Trifluoromethyl-phenyl)-4,5,6,7-tetrahydro-benzothiazol-4-ylmethoxy]-phenyl}-acetic acid;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(R)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

(S)-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethoxy]-phenyl}-propionic acid;

{3-[2-(4-Trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethoxy]-phenyl}-acetic acid;

(R)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

(S)-3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-4H-cycloheptathiazol-4-ylmethylsulfanyl]-phenyl}-propionic acid;

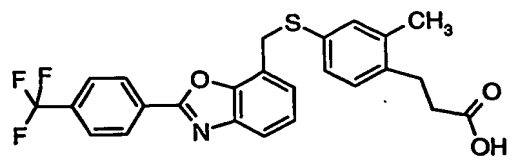
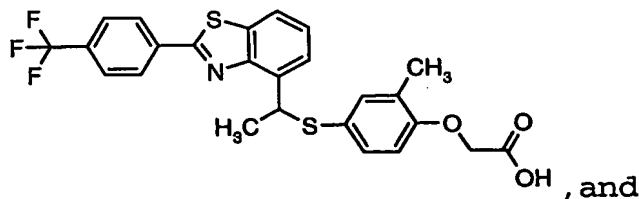
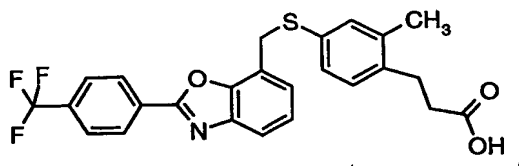
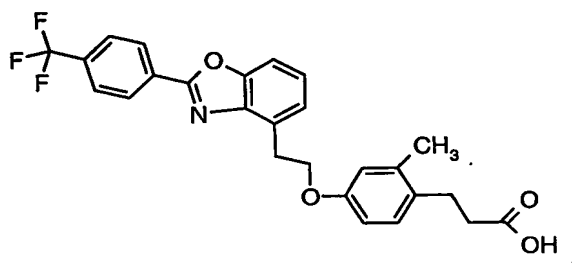
{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-4,5,6,7,8,9-hexahydro-cyclooctathiazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid;

{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic
acid;
{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethylsulfanyl]-phenoxy}-acetic
acid ethyl ester;
3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethylsulfanyl]-phenyl}-propionic
acid;
{3-[2-(4-Trifluoromethyl-phenyl)-benzothiazol-4-
ylmethoxy]-phenyl}-acetic acid;
3-{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;
(S)-2-Methoxy-3-{4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethoxy]-phenyl}-propionic acid;
2-Methyl-2-{2-methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethoxy]-phenoxy}-propionic acid;
Racemic-(2-methyl-4-{1-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-yl]-ethylsulfanyl}-phenoxy)-acetic
acid; and
Racemic-3-(2-methyl-4-{1-[2-(4-trifluoromethyl-
phenyl)-benzothiazol-4-yl]-ethylsulfanyl}-phenyl)-
propionic acid.

55. A compound as claimed by any one of Claims 1
through 4 which is selected from the group
consisting of {2-Methyl-4-[2-(4-
trifluoromethyl-phenyl)-benzothiazol-4-
ylmethylsulfanyl]-phenoxy}-acetic acid and 3-
{2-Methyl-4-[2-(4-trifluoromethyl-phenyl)-
benzothiazol-4-ylmethylsulfanyl]-phenyl}-
propionic acid.

56. A compound as claimed by any one of Claims 1
through 4 selected from the group consisting of

2-Ethyl-4-[2-(4-trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanylphenoxyacetic Acid; 3-[2-(4-Trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanyl-phenylacetic Acid; 6-[2-(4-Trifluoromethylphenyl)benzothiazol-4-ylmethylsulfanyl]benzo[b]thiophen-3-yl}acetic Acid; 2-Ethyl-4-[2-(4-trifluoromethylphenyl)benzothiazol-7-ylmethylsulfanyl]phenoxyacetic Acid; and 2-Ethyl-4-[2-(4-trifluoromethylphenyl)-3H-imidazo[4,5-b]pyridin-7-ylmethylsulfanyl]phenoxyacetic Acid,



57. A compound as claimed by any one of Claims 1 through 55 that is in the S conformation.

58. A compound as claimed by any one of Claims 1 through 55 that is in the R conformation.

59. A pharmaceutical composition, comprising as an active ingredient, at least one compound as claimed by any one of Claims 1 through 58 together with a pharmaceutically acceptable carrier or diluent.

60. A method of modulating a peroxisome proliferator activated receptor, comprising the step of contacting the receptor with at least one compound as claimed by any one of Claims 1 through 58.

61. A method of treating diabetes mellitus in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 58.

62. A method of treating Metabolic Syndrome in a mammal, comprising the step of administering to the mammal in need thereof a therapeutically effective amount of at least one compound of Claims 1 through 58.

63. A method of selectively modulating a PPAR delta receptor comprising administering a compound as claimed by any one of Claims 1 through 58 to a mammal in need thereof.

64. The manufacture of a medicament for use in the treatment and/or prevention of a condition mediated by nuclear receptors, in particular by a peroxisome proliferator activated receptor, wherein the compound is a compound as claimed by any one of Claims 1 through 58.

65. A method for treating or preventing the progression of cardiovascular disease in a mammal in need thereof comprising administering a therapeutically effective amount of a compound as Claimed by any one of Claims 1 through 58.

66. A method as claimed by Claim 65 wherein the mammal is diagnosed as being in need of such treatment.

67. A method of treating arthritis in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

68. A method of treating demyelating disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

69. A method of treating inflammatory disease in a mammal, comprising the step of administering to the mammal in need thereof, a therapeutically effective amount of at least one compound as claimed by any one of Claims 1 through 58.

70. A method as claimed by any one of Claims 67, 68, and 69 wherein such mammal is diagnosed as being in need of such treatment.

71. A compound as Claimed by any one of Claims 1 through 58 for use as a pharmaceutical.

72. A compound as claimed by any one of Claims 1 through 58 wherein the compound is radiolabeled.

73. A compound as disclosed by any one of the Examples herein.

74. All methods disclosed herein of preparing the compounds as claimed by any one of Claims 1 through 4.